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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/621,592	07/21/00	JACKOWSKI G	SKP002

HM22/1003

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EXAMINER	
COOK, L	
ART UNIT	**PAPER NUMBER**
1641	4

DATE MAILED: 10/03/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/321,592	George Jackowski
Examiner	**Group Art Unit**
Lisa V. Cook	1641

☒ Responsive to communication(s) filed on *Jul 21, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *21-33* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *21-33* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☒ received in Application No. (Series Code/Serial Number) *09/510,700*.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 7/21/00 in Paper #2 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(b) based on parent Application No. 09/510,700 is acceptable and a CPA has been established. An action on the CPA follows.

Claims 1-20 were cancelled pursuant to Applicants' request filed in Paper #2, page 2, and item 5. Currently, claims 21-33 are pending and under consideration.

Priority

2. Receipt is acknowledged of papers(Application No. 2,263,063 filed in Canada) submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the parent Application No. 09/510,700.

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). The instant application does not contain the required first referencing Canadian Application no. 2,263,063. Please add to the specification.

Drawings

4. The drawings in this application are objected to by the Draftsperson as informal. Any drawing corrections requested, but not made in the prior application should be repeated in this application if such changes are still desired.

If the drawings were changed and approved during the prosecution of the prior application, a petition may be filed under 37 CFR 1.182 requesting the transfer of such drawings, provided the parent application has been abandoned. However, a copy of the drawings as originally filed must be included in the 37 CFR 1.60 application papers to indicate the original content.

Information Disclosure Statement

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

Oath/Declaration

6. A new oath or declaration is required because it does not identify the post office address of each inventor. A post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The post office address should include the ZIP Code designation. The inventors' full address appears to be 17725 Keele St., Kettleby, Ontario, Canada L0G 1JC and this address has not been properly executed in the oath.

The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Specification

7. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

8. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should appear in upper case, without underlining or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.
(b) Cross-References to Related Applications.
(c) Statement Regarding Federally Sponsored Research or Development.
(d) Reference to a "Microfiche Appendix" (see 37 CFR 1.96).
(e) Background of the Invention.
    1. Field of the Invention.
    2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.

(f) Brief Summary of the Invention.
(g) Brief Description of the Several Views of the Drawing(s).
(h) Detailed Description of the Invention.
(i) Claim or Claims (commencing on a separate sheet).
(j) Abstract of the Disclosure (commencing on a separate sheet).
(k) Drawings.
(l) Sequence Listing (see 37 CFR 1.821-1.825).

In the instant application, the Brief Description of the Drawings is misleading. On page 6, lines 4 and 5 of the disclosure figures 3-10 are represented by one description which implies that each of the graphs are identical or have minimal differences so as to constitute their grouping. However, the figures are further described on pages 25 and 26 of the disclosure and taught to be substantially different-data from different patients exemplifying different events. It is recommended that the clarified descriptions on page 25-26 for each figure 3-10 be incorporated into section (g) Brief Description of the Drawings. See MPEP 608.01(f).

Also, the instant application appears to have several related applications/patents that were not incorporated into section (b) Cross-References to Related Applications. (i.e. USP#s: 5,744,358 - 5,747,274 – 5,604,105 – 5,710,008 –5,290,678 – Application #s: 08/026,453 – 08/481,743).

9. The use of several trademarks is noted in this application. They should be capitalized wherever they appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. (For example, see page 14 – OPUS®, OPUS MAGNUM® etc).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 21-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 23 is vague and indefinite in utilizing the phrase "blood products". Because the term is not defined in the disclosure the metes and bounds can not be determined. Is it applicants' intent to claim any material containing blood, any product useful in blood analyses, or any product derived from blood? Please clarify.

B. In claim 28, the use of "same sample" is vague and indefinite because it is unclear as to what is encompassed by the phrase. Is the "same sample" wording directed to separate aliquots from the same sample wherein the reaction for each marker is separately analyzed or does same sample refer to a single reaction wherein all the markers are added to a single sample? On page 16, line 1, of the specification, samples were centrifuged and aliquots of serum were frozen for further analyses. If applicant intends to claim <u>same sample aliquots</u> it is suggested that the claim language recite this to eliminate any ambiguity.

C. Claim 24 is vague and indefinite in the use of the acronym HT7. Is the term to be defined by any prior art teaching? The term should be defined in its first instance. This initial explanation will convey intended meaning with subsequent abbreviations. Please identify applicants intended meaning.

D. Claims 21 and 24 recite "combinations thereof". It is not clear as to what combinations are being claimed. It appears that any combination of any of the recited proteins or any additional composition containing any of the recited proteins would meet the limitation of this claim. No specific guidance was provided through a clear definition of what "combinations thereof" is meant to entail. Please explain.

E. Claims 26 and 27 are drawn to a method that requires a secondary marker with the "same specific cell type" as the other markers utilized in the method. This claim is vague and indefinite because it is not clear as to what "specific cell type" applicant is referring. It is suggested that applicant include the specific cell type to obviate this rejection.

11. Claims 21-33 (specifically claims 21) are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. There are no claimed steps reciting the washing or removal of unbound materials. If no separation will be performed it is

unclear how the complex will be identified from the reaction solution containing both bound ad unbound material. Further, there are no steps that identify reagent and sample contact thereby forming a detectable complex which is correlated to the diagnosing and distinguishing of stroke as recited in the preamble.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 21-33 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The methods/kits of independent claims 1 and 14 have insufficient steps. These critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Merely, reciting the use of reagents in an assay format is not considered a proper method step. An assay as recited in the preambles of claims 1 and 14, requires at least a contact step between reagent and sample – resulting in binding/complex formation, separation, detection, and a correlation step directed to the analysis of interest. The recited claims do not include the required steps for contact, formation, separation, detection and correlation. There are no claimed steps reciting the washing/removal of unbound material. With respect to claims 1 and 14, a separation step that removes unbound reagents from the formed measurable complex is missing. If you do not have a separation step after complex

formation, the addition of materials will always provide a positive result regardless of the amount of ligand bound to the antibodies in the formed complex and thus could not be utilized to detect the ligand or correlate it to an event. The presence of unbound materials is also a serious problem in view of the detection step, which is directed to quantitating the marker present in a sample as an indicator (diagnosing and distinguishing) of stroke. The presence of the unbound materials will generate a greater detection signal as an indication of stroke than is actually present in the sample. Please add the removal of unbound label to the claims or clearly indicate the specific method of detection that does not employ the removal of unbound material.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-33 are rejected under 35 U.S.C.103(a) as being unpatentable over Jackowski (U.S. Patent # 5,604,105) or Jackowski (U.S. Patent # 5,710,008 in view of Strand et al. (Stroke, Dallas, 1984, 15(10, pages 138-44), Fassbender et al. (J. Neurol. Science, 1997, 148(1), pages 101-105), Huguet (Lyon Pharm, 1993, 44(3), pages 187-

44(3), pages 187-92-Abstract Only), Sulter et al. (Neurosci. Letters, 1988, 253(1) pages 71-73), or Yatsu et al. (Stroke, 1995, Vol.26, No.1, page 177).

Jackowski (5,604,105) teaches a method which detects a minimum of three markers that together present data distinguishing between ischemic and non-ischemic events. (Column 9, lines 64-67). A sample such as blood is contacted with antibodies specific for at least three markers to form a binding partner-marker binding pair. This complex is reacted with a second capture antibody to form a multiple antibody-marker composition. Each of the markers are then simultaneously assessed to ischemic events. (column 10, 17-62).

Jackowski (5,710,008) also disclose methods and kits to detect at least three different markers of ischemic disorders. In one embodiment the first marker is an ischemic marker, and the other two markers are specific for myocradial infarction. (column 20, lines 34-51). Several ischemic markers and their time of appearance in cardiac events is listed in Table 3.

Jackowski (5,604,105) and Jackowski(5,710,008) differ from the instant invention in not teaching the use of stroke specific markers as defined by claim 1, step a.

However, each of the recited markers (i-iv) are well known in the art and have been shown to correlated well with stroke events. This fact is supported by the following references:

Regarding, myelin basic protein, Strand et al. (Stroke) teach that myelin basic protein measurement is a good marker for predicting cerebral damage after stroke or cerebral hemorrhage (see abstract).

In the case of the S100 protein, Fassbender et al. (Journal of Neurol. Science) teach that serial quantification of S-100 in peripheral blood sample both acute and subacute phases of ischemic stroke is a significant measure of infarctions while control patient samples did not contain detectable S-100 (see abstract).

Neuron-Specific enloase (NSE) is disclosed by the reference of Huguet (Lyon Pharm.) as a significant tumor marker and possible indicator of neuronal damage in stroke patients (see abstract). Sulter et al. (Neurosci. Letters) also disclosed the utility of neuron specific enolase concentrations as a measure for ischemic stroke.

Lastly, Yatsu et al. (Stoke) identified Brain endothelial cells as an important protein in stroke measurements (see abstract).

Therefore, it would have been obvious at the time of applicants' invention to used known markers for stroke (namely, myelin basic protein, S100 protein, neuronal specific enolase, and brain endothelial cells as taught by Strand et al., Fassbender et al, Huguet et al., Sulter et al., or Yatsu et al. in either method of Jackowski (5,604,105) or Jackowski(5,710,008) because both methods of Jackowski teach that "many ischemic markers to which antibodies have been produce are well known in the art. (USP5,604,105-Column 2, lines 28-30).

One having ordinary skill in the art would have been motivated to do this because Jackowski (5,604,105) and Jackowski(5,710,008) taught that their method was rapid, accurate, sensitive, and could distinguish an ischemic event. (USP5,604,105-Column 9, lines 44-62)

14. For reasons aforementioned, no claims are allowed.

Remarks

15. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Jackowski (USP# 5,290,678) teach kits that are employed in diagnosing and distinguishing chest pain of cardiac origin from other events. (Abstract)

B. Jackowski (USP# 5,744,358 and 5,747,274) disclose methods and devices that are utilized in assessing cardiac evaluations.

16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7D16
(703) 305-0808
9/28/00

RODNEY P. SWARTZ, PH.D
PRIMARY EXAMINER